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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/056,072	04/07/1998	HERVE BAZIN	61750221	4832

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EXAMINER	
GAMBEL, PHILLIP	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/056,072	BAZIN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-36,38-42 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44* is/are allowed.

6)☒ Claim(s) *30-36, 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 05/08/2008 has been entered.

Claims 30-36, 38-42 and 44 are pending and being acted upon.

Claims 1-29, 37 and 43 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Office Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 05/08/2008.

The rejections of record can be found in the previous Office Actions.

Once again, applicant's arguments and the examiner's rebuttal appear to be essentially the same of record.

3. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Once again, applicant is reminded of the following.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825

Applicant is required to amend the specification (e.g. see Brief Description of the Drawings, particularly Figures 29-34) to indicate the appropriate SEQ ID NOS.

Applicant is reminded that the following and should amend the specification accordingly (e.g. see page 12 of the instant specification).
The current address of the ATCC is as follows:
American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

4. Claims 30-32 and 35-36 stand rejected under 35 U.S.C. 102(b) as being anticipated by Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990) for the reasons of record alone
Or in further evidence of Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 148-153) (892 mailed 11/02/2006)
and Wallace et al. Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 120-123) essentially for the reasons of record.

Applicant's arguments in conjunction with certain legal citations, filed 05/08/2008, and the Bierer Declaration, filed 01/04/1999 have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant's arguments and the examiner rebuttal are essentially the same of record, which is addressed and reiterated herein.

Again it is noted that applicant appears to ignore that this rejection of record is consistent with the Decision on Appeal in Ex parte HERVE BAZIN and DOMINIQUE LATINNE, mailed 07/31/2003, of the instant application USSN 09/056,072.

Given that Applicant's arguments and the examiner rebuttal are essentially the same of record, the following of record is essentially reiterated herein.

In contrast to applicant's assertions that Xia provides no information with respect to the epitope to which Lo-CD2A binds,
the rejection of record (reiterated herein) has supported that Xia et al. provides for sufficient information with respect to the epitope that LO-CD2a binds.

In contrast to applicant's focusing in on the common properties of anti-CD2 antibodies (e.g., antibodies that bind CD2);
applicant continues to ignore the prior art teaching, including Xia et al., does distinguish CD2 epitopes by binding and functional properties / characteristics, including the epitope bound by the LO-CD2 antibody.

While applicant notes that Wallace and Olive et al. do not disclose the LO-CD2 antibody,
the following of record is reiterated as that Wallace and Olive et al. were included in the rejection of record to address continual assertions concerning epitopes.

Given applicant's continual insistence that the prior art Xia et al. does not anticipate the instant claims,
Olive et al. and Wallace et al. were added to provide further evidence that the classification of anti-CD2 antibody epitopic specificities can be and have been established via the combined data obtained through binding assays, including tissue distribution, as well as functional assays.

Further, it was noted that Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 148-153) (892 mailed 11/02/2006) is the same citation relied upon the Bierer Declaration of record and previously addressed herein.

The 1987 publications of Olive et al. and Wallace et al. clearly provide for the prior art recognition that anti-CD2 antibody epitopic specificities can be and have been established via the combined data obtained through binding assays, including tissue distribution, as well as functional assays and that anti-CD2 antibodies can be divided into epitope groups (see entire documents, including page 148, column 1, paragraph 3 of Olive et al. and page 120, column 1, paragraph 1 of Wallace et al.).

Again, as indicated previously in response to applicant's reliance upon Olive et al. in the Bierer Declaration that one would not be able to identify LO-CD2-specific antibodies,
it appears that even among these CD2-specific antibodies referred to Table 1 (page 149) of the Third International Workshop;
these antibodies do not have the same or identical characteristic profiles and that these profiles can be distinguished from all of the characteristics of the LO-CD2a-specificity set forth in Xia et al.

Once again, applicant's analysis, in conjunction with the Bierer Declaration, of the prior art, including the characteristics set forth in the Tables and Figures of Xia et al. and the examiner's rebuttal are the same of record and reiterated below in rejection of record.

Again, applicant's assertions that the prior art of Xia et al. does not provide for an antibody that necessarily or inherently binds to the same epitope as the LO-CD2a antibody deposited as ATCC HB 11423
or that the prior art of Xia et al. would not be able to identify which of the antibodies was LO-CD2a or antibody which binds to the same epitope as the deposited antibody
or that the prior art Xia et al. does not identify the LO-CD2a antibody uniquely
has been acknowledged.

However, as noted previously as well as the Board of Appeals Decision on Appeal in Ex parte HERVE BAZIN and DOMINIQUE LATINNE, mailed 07/31/2003, of the instant application USSN 09/056,072,
applicant is reminded that the instant claims are drawn to a genus of antibodies that bind the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423.

While it may be true that a person of ordinary skill in the art could not reasonably expect to produce the particular LO-CD2a antibody species that is exactly the same, both chemically and structurally, as an antibody produced by a specific deposited cell line,
given the high polymorphism of antibodies;
the claimed genus of antibodies bind the same epitope as the LO-CD2a antibody is not so limited in terms of chemistry or structure.

Therefore, any antibody that is capable of binding the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423 meets the limitations of the instant claims.

On this record, Xia et al. teach antibodies that bind the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423.

In contrast to applicant's assertions that Xia et al. merely teaches that LO-CD2 antibody is an antibody that bind to CD2 or that LO-2 antibody has characteristics which are common to anti-CD2 antibodies as a class,
the teachings of Xia et al., including the Tables and Figures, provide for a profile of binding specificities and functional properties both in a quantitative and qualitative manner that distinguish the LO-CD2a antibody specificity from other anti-CD2 antibodies.

In contrast to applicant's assertions that the prior art does demonstrate that the ordinary artisan necessarily would be able to obtain the claimed antibody and the prior art rejection is based upon speculation only,
it continues to be maintained that Xia et al. does provide sufficient information to distinguish the LO-CD2a antibody specificity from other anti-CD2 antibodies at the time the invention was made or that identifying the particular LO-CD2a antibody uniquely was not required to identify the LO-CD2a antibody specificity at the time the invention was made
and that the burden has been properly shifted to applicant in this matter.

Therefore, any antibody that is capable of binding the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423 meets the limitations of the instant claims.

On this record, Xia et al. teach antibodies that bind the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423.

This rejection is consistent with the Decision on Appeal in Ex parte HERVE BAZIN and DOMINIQUE LATINNE, mailed 07/31/2003, of the instant application USSN 09/056,072.

As indicated previously, given applicant's continual insistence that the prior art Xia et al. does not anticipate the instant claims,

Olive et al. and Wallace et al. have been added herein to provide further evidence that the classification of anti-CD2 antibody epitopic specificities can be and have been established via the combined data obtained through binding assays, including tissue distribution, as well as functional assays.

Further, it has been noted that Olive et al. Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 148-153) (892 mailed 11/02/2006) is the same citation relied upon the Bierer Declaration of record and previously addressed herein.

The 1987 publications of Olive et al. and Wallace et al. clearly provide for the prior art recognition that anti-CD2 antibody epitopic specificities can be and have been established via the combined data obtained through binding assays, including tissue distribution, as well as functional assays and that anti-CD2 antibodies can be divided into epitope groups (see entire documents, including page 148, column 1, paragraph 3 of Olive et al. and page 120, column 1, paragraph 1 of Wallace et al.).

As indicated previously in response to the reliance upon Olive et al. in the Bierer Declaration,

it appears that even among these CD2-specific antibodies referred to Table 1 (page 149) of the Third International Workshop;

these antibodies do not have the same or identical characteristic profiles and that these profiles can be distinguished from all of the characteristics of the LO-CD2a-specificity set forth in Xia et al.

In contrast to applicant's assertions, Xia et al. does provide sufficient information to distinguish the LO-CD2a antibody from other anti-CD2 antibodies at the time the invention was made or that Xia et al. does not provide information that identifies the LO-CD2a antibody uniquely.

The following of record is reiterated for applicant's convenience.

Xia et al. teach the LO-CD2a-specificity, including hybridomas and methods of making said antibodies and hybridomas of the instant invention (see entire document and page 312 for example).

Again, applicant is invited to see the Examiner's Answer, mailed 8/24/2000, for a more complete analysis of applicant's arguments and the examiner's rebuttal.

Once again, applicant's arguments, filed 11/02/2007, including reliance upon the 132 Bierer Declaration and newly amended claims reciting "an antibody which elicits alloantigen specific hyporesponsiveness" and the examiner's rebuttal are essentially the same of record.

Again, applicant asserts that the burden is upon the examiner show that Xia et al. discloses all of the elements and limitations of applicant's claimed antibody, that is, an antibody that binds the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423 and an antibody which elicits alloantigen specific hyporesponsiveness.

Again, applicant appears to assert that Xia et al. is limited to standard procedures of producing anti-CD2 antibodies, which would resulted in producing a myriad of anti-CD2 antibodies, with no evidence that the ordinary artisan would be able to obtain and claimed antibody specificity from a wide variety of other possible antibodies.

Again, it appears that applicant is asserting that the totality of the references, including the Bierer Declaration, indicate that the characteristics disclosed by Xia et al. are not sufficient to identify LO-CD2 in a manner that distinguishes LO-CD2 from CD2 antibodies as a class or enables the ordinary artisan to identify antibodies which binds to the same epitope as the antibody produced by the deposited cell line.

Again, in contrast to appellant's arguments, including applicant's arguments that the anticipatory rejection under 35 USC 102 must necessarily be present rather than relying upon mere probabilities or possibilities;

Xia et al. teach the LO-CD2a-specificity and rely upon a number of characteristics to distinguish this specificity (see entire document, including Tables 1-6 and Figures 1-4), including distinguishing the LO-CD2 specificity from other CD2-specific antibodies (see page 320, paragraphs 1-3).

Here again in Xia et al.; the Tables and Figures provide for a profile of binding specificities and functional properties both in a quantitative and qualitative manner. For example, Tables 1-4 and Figures 1-4 provide for reactivity patterns of antibodies that provide for intensity of binding in addition to binding specificity.

Here, the LO-CD2 antibody specificity is compared with another anti-CD2 antibody specificity, namely the OKT11/T11 antibody (See Tables and Figures).

Xia et al. discloses that reactivity patterns of LO-CD2 antibody and OKT11 exhibit similarities; they are not considered identical. See page 320, paragraph 1.

Here, the difference between LO-CD2 and OKT11 is that LO-CD2 always show a weaker reaction with T lymphocytes than T11 and that LO-CD2 did not react with T cell line CEM, while OKT11 did.

Xia et al. distinguish the epitope recognized by another CD2 antibody, namely D66, based upon functional characteristics of blocking E-rosette formation. See page 320, paragraph 2.

LO-CD2 was also compared with non-CD2-specific antibodies, wherein the effect of LO-CD2 was in sharp contrast to that of CD25-specific antibodies. See page 320, paragraph 4.

As noted previously, Section 4 of the Bierer Declaration asserts that reactivity patterns in Figures 1A/1B is not statistically different from another CD2 antibody, namely OKT11.

However, as pointed out above; Xia et al. do not rely upon Figures 1A/1B alone to distinguish LO-CD2 from OKT11. Here, the difference between LO-CD2 and OKT11 is that LO-CD2 always show a weaker reaction with T lymphocytes than T11 and that LO-CD2 did not react with T cell line CEM while OKT11 did.

Section 16 of the Bierer Declaration relies upon the Third International Workshop and Conference on Human Leukocyte Differentiation Antigens, 1986 (page 149) to indicate that several CD2 antibodies which did not react with CEM cells, did react with MOLT4 cells, HPB-ALL cells and Jurkat cells, whereby the reactivity patterns of Table 4 is not unique to LO-CD2.

It appears that even among these CD2-specific antibodies referred to Table 1 (page 149) of the Third International Workshop; these antibodies do not have the same or identical characteristic profiles that these profiles can be distinguished from all of the characteristics of the LO-CD2a-specificity set forth in Xia et al.

Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Here again, the prior art as a whole includes teaching antibodies that bind the same epitope with functional characteristics that are consistent with the claimed invention, including the newly added recitation of "where the antibody elicits alloantigen specific hyporesponsiveness.

Giving the claims the broadest reasonable interpretation, see In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (during ex parte prosecution, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification),
the claims read on "an antibody which elicits alloantigen specific hyporesponsiveness", wherein there is a resultant inhibition or reduction of alloantigen specific responsiveness. The claims do not specify any level of inhibition or reduction, thus the claims read on any measurable inhibition or reduction of alloantigen specific unresponsiveness. In addition, the antibody must bind the same epitope as the LO-CD2a antibody.
However, there is no requirement that the antibody elicit alloantigen specific unresponsiveness to the extent of the LO-CD2a antibody exemplified in instant Example 8.

Further, it is noted that Xu et al. (Clin. Exp. Immunol. 138: 476-483, 2004) (of record and cited by applicant in response to a prior art rejection) notes that is remains to be established whether specific unresponsiveness as observed in the MLR secondary response also occurs in vivo following treatment with BTI-322 or its human analogue (see page 483, column 1, paragraph 1). Here, too, Xu et al. notes it is difficult to assess the specific role of the antibody in the induction of tolerance. The Discussion of Xu et al. also notes that the intact BTI-322 molecule is also required (see page 482, column 2).

Thus, in addition to binding the same epitope as the LO-CD2 antibody, all that is required is that the antibody elicit some degree of alloantigen specific unresponsiveness with any measurable level of specificity.

Also, as pointed out previously in contrast to applicant's assertions and as noted in the Decision on Appeal by the BPAI, mailed 07/31/2003;
Xia et al. teach the LO-CD2a antibody, subsequently deposited as ATCC HB 11423, teaches the methodology of producing antibodies and hybridomas, and teach the reactivity pattern of LO-CD2a with normal and leukemic cells.

Applicant submits that the no evidence of record has been provided which indicates that the LO-CD2a antibody as described by Xia was available to the public prior to the effective filing date of the instant application.
Applicant asserts that the ordinary artisan would not have been enabled to obtain the necessary antibody which binds the same epitope of the deposited antibody.

However, the proper issue is whether the prior art is enabling in the sense that is describes the claimed invention sufficiently to enable a person of ordinary skill in the art to carry out the invention.
For example, see Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc., 81 USPQ2d 1001 (Fed. Cir. 2006).

Also, it is noted that a reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).
See MPEP 2121.01.

Also, as noted on page 8 the Decision on Appeal by the BPAI, mailed 7/31/2003;
"As a whole, we are not persuaded by either appellant's Brief or the Bierer declaration. While the Brief relies heavily on the Bierer declaration, Bierer discusses Xia's tables individually, and fails to address the significance of the data when viewed as a whole. As the examiner explains (Answer, page 9), "it is the totality of the reactivity patterns and functional characteristics, clearly disclosed in Xia et al. that serves to distinguish the LO-CD2[a] antibody specificity over the prior art and not just binding to one cell line or even a few binding characteristics."

Again, it is the totality of the reactivity patterns and functional characteristics clearly disclosed in Xia et al. that serves to distinguish the LO-CD2a antibody specificity over the prior art and not just binding to one cell line or even a few binding characteristics.

Given all of the criteria of the anti-LO-CD2a antibody specificity clearly taught and enabled by the prior art Xia et al. teaching; the ordinary artisan would have been enabled to making and using antibodies which bind the same LO-CD2a epitope encompassed by the claimed invention.

While the characteristics disclose by the prior art may be common to certain classes of CD2-specific antibodies, this reference clearly distinguishes the LO-CD2a antibody specificity from other CD2-specific antibodies, including providing a profile of a number of characteristics and comparisons for antibodies that bind the same epitope as the LO-CD2a antibody.

With respect to applicant's assertions that nothing in the record would indicate that because LO-CD2a antibody produced by Xia et al. would necessarily be produced again by the referenced methods,
again applicant is reminded that the rejection is not directed towards the LO-CD2a antibody per se.

Again as noted previously and above herein,
applicant is reminded that the prior art rejection is based upon antibodies that bind the same epitope as the LO-CD2a antibody rather than based upon producing the LO-CD2a antibody itself or other LO-CD2a-specific antibodies with the same exact chemical structure as the LO-CD2a antibody.

Therefore, instant claims stand rejected under 35 U.S.C. § 102(b) as being anticipated by Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990).

The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965).

Applicant's arguments have not been found persuasive.

5. Claims 30-36 and 38-42 are rejected under 35 U.S.C. 103 as being unpatentable over Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990) in view of Queen et al. (U.S. Patent No. 5,530,101) or Newman et al. (U.S. Patent No. 5,658,570) and in further view of Guckel et al. (J. Exp. Med., 1991) OR Bromberg et al. (Transplant., 1991) OR Hafler et al. (J. Immunol., 1988) OR Chavin et al. (Transplant., 1992) OR Faustman (U.S. Patent No. 5,283,058) essentially for the reasons of record.
and/or in further evidence of Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 148-153) (892 mailed 11/02/2006)
and Wallace et al. Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 120-123) for the reasons of record.

Applicant's arguments in conjunction with certain legal citations, filed 05/08/2008, and the Bierer Declaration, filed 01/04/1999 have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant's arguments and the examiner rebuttal are essentially the same of record, which is addressed and reiterated herein and above in the rejection under 35 USC 102.

See Section 4 above for additional comments concerning applicant's latest response.

The following of record is reiterated for applicant's convenience.

As indicated above, applicant's assertions that the prior art of Xia et al. does not provide for an antibody that necessarily or inherently binds to the same epitope as the LO-CD2a antibody deposited as ATCC HB 11423 or that the prior art of Xia et al. would not be able to identify which of the antibodies was LO-CD2a or antibody which binds to the same epitope as the deposited antibody are acknowledged.

Again, applicant is reminded that the instant claims are drawn to a genus of antibodies that bind the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423.
While it may be true that a person of ordinary skill in the art could not reasonably expect to produce the particular LO-CD2a antibody species that is exactly the same, both chemically and structurally, as an antibody produced by a specific deposited cell line,
given the high polymorphism of antibodies;
the claimed genus of antibodies bind the same epitope as the LO-CD2a antibody is not so limited in terms of chemistry or structure.

Therefore, any antibody that is capable of binding the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423 meets the limitations of the instant claims.

On this record, Xia et al. teach antibodies that bind the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423.

Again, this rejection is consistent with the Decision on Appeal in Ex parte HERVE BAZIN and DOMINIQUE LATINNE, mailed 07/31/2003, of the instant application USSN 09/056,072.

Given applicant's continual insistence that the prior art Xia et al. does not anticipate the instant claims,
Olive et al. and Wallace et al. were added herein to provide further evidence that the classification of anti-CD2 antibody epitopic specificities can be and have been established via the combined data obtained through binding assays, including tissue distribution, as well as functional assays.

Further, it is noted that Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, Great Britain, 1987; pages 148-153) (892 mailed 11/02/2006) is the same citation relied upon the Bierer Declaration of record and previously addressed herein.

The 1987 publications of Olive et al. and Wallace et al. clearly provide for the prior art recognition that anti-CD2 antibody epitopic specificities can be and have been established via the combined data obtained through binding assays, including tissue distribution, as well as functional assays and that anti-CD2 antibodies can be divided into epitope groups (see entire documents, including page 148, column 1, paragraph 3 of Olive et al. and page 120, column 1, paragraph 1 of Wallace et al.).

As indicated previously in response to the reliance upon Olive et al. in the Bierer Declaration,
it appears that even among these CD2-specific antibodies referred to Table 1 (page 149) of the Third International Workshop;
these antibodies do not have the same or identical characteristic profiles that these profiles can be distinguished from all of the characteristics of the LO-CD2a-specificity set forth in Xia et al.

In contrast to applicant's assertions, Xia et al. does provide sufficient information to distinguish the LO-CD2a antibody from other anti-CD2 antibodies at the time the invention was made.

In addition, the following of record is reiterated from previous Office Actions for applicant's convenience.

Applicant's arguments in conjunction with the Bierer Declaration filed in priority USSN 08/472,281, now U.S. Patent No. 5,817,311, filed 02/04/2005, and relied upon in applicant's current amendment, filed 11/02/2007, have been fully considered but have not been found convincing essentially the same of record.

Applicant's arguments, including the Bierer Declaration of record as well as the newly amended recitation of "an antibody which elicits alloantigen specific hyporesponsiveness" and the examiner's rebuttal are essentially the same of record and/or addressed above.

Thus, in addition to binding the same epitope as the LO-CD2 antibody; all that is required is that the antibody elicit some degree of alloantigen specific unresponsiveness with any measurable level of specificity.
See applicant's arguments and the examiner's rebuttal concerning antibody specificity (e.g., epitope and elicitation of alloantigen specific hyporesponsiveness), including the issues of enabling prior art in Section 4 above.

Applicant's reliance upon the Bierer Declaration has been fully considered but has not been found convincing essentially for the reasons of record, which has been addressed as well in the rejection under 35 USC 102 as well as in the Decision on Appeal by the BPAI, mailed 7/31/2003, of record.

Here, applicant in conjunction with the Bierer Declaration appear to simply reiterate that the prior art does not provide sufficient teachings for the ordinary artisan to identify an antibody which has the characteristics similar to those of LO-CD2a in Xia et al.

The following of record is reiterated for applicant's convenience, wherein the rejection of record provides sufficient motivation and expectation of success in deriving immunosuppressive and therapeutic amounts of anti-CD2 antibodies, including antibodies that bind the same epitope as the LO-CD2a antibody.
Also, note as addressed above that in addition to binding the same epitope as the LO-CD2 antibody, all that is required is that the antibody elicit some degree of alloantigen specific unresponsiveness with any measurable level of specificity.

The instant claims are drawn to antibodies that bind the LO-CD2a specificity, including chimeric and humanized antibodies, as well as cell that produced said antibodies and methods of making said antibody.

Xia et al. provides a number of phenotypic and functional characteristics that are associated with the LO-CD2a specificity (see entire document). Also, Xia et al. distinguishes the LO-CD2a specificity from other CD2-specific antibodies and clearly discloses that this specificity binds a different epitope from other CD2-specific antibodies (for example, see page 320, paragraphs 1-3). It would have been expected at the time the invention was made that different antibodies would recognize the same conformational epitope, which is the LO-CD2a epitope in the instant case. The prior art clearly set forth numerous features that characterize and enable one of skill in the art at the time the invention was made to make an antibody that binds to the same LO-CD2 epitope specificity as claimed. Xia et al. differs from the instant claims by not disclosing chimeric or humanized antibodies per se.

Queen et al. teaches the art-known procedures at the time the invention was made to produce chimeric antibodies starting from hybridoma and antibody producing cells (see entire document)..

Similarly, Newman et al. teach the generation of recombinant antibodies including CD2-specific antibodies for various diagnostic and therapeutic uses (see entire document). While it is noted that Newman et al. teaches the use of Old World Monkey portions in the derivation of recombinant antibodies, this reference clearly recognizes the derivation of chimeric and humanized antibodies at the time the invention was made and that CD2 was a desired specificity at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have generated chimeric or humanized antibodies in order to reduce immunogenicity while retaining high binding affinity for diagnostic and therapeutic purposes as well as the appropriate vectors, host cells, etc. to accomplish the engineering of chimeric and humanized antibodies (see entire documents). Therefore, Queen et al. OR Newman et al. teach that immunoglobulin gene structure and organization were well understood in the art at the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs comprising expression vectors containing DNAs encoding immunoglobulin variable regions. Queen et al. AND Newman et al. differ from the claimed invention by not teaching the LO-CD2a specificity per se, the ordinary artisan would have been motivated to apply the teachings of Queen et al. OR Newman et al. to enable the isolation and construction of chimeric and humanized antibodies that bind the LO-CD2a specificity.

In addition to the LO-CD2a specificity, the instant claims also encompass antibodies that elicit alloantigen specific unresponsiveness. Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman all teach the art-known potent inhibition of immune responses by blocking or modulating T cell surface receptors such as CD2 that are important in adhesion receptor-signaling (see entire documents, particularly the Introductions and Discussions).

Guckel et al. teach the ability of rat anti-CD2 antibodies to induce T cell unresponsiveness in vitro and in vivo in mice (see entire document). CD2-specific antibody inhibition of transplants and autoimmunity is taught (page 965, column 2, paragraph 2). Guckel et al. Also teach that CD2 modulation was dose and time dependent, whereby a single dose of 0.1 – 5 mg purified antibody resulted in maximal modulation within 24 hours (see page 964, column 1, paragraph 1).

Bromberg et al. teach that anti-CD2 antibodies alter cell-mediated immunity, such as contact sensitivity and CTL responses in vivo by altering the array of cell surface receptors and subsequent responses to antigenic challenge (see entire document). Additional experiments showed a well-defined dose-response relationship between the amount of anti-CD2 administered and subsequent immunosuppression (see Abstract on page 219, column 1). Bromberg et al. also teach the potent immunosuppressive properties of anti-CD2 antibodies for murine allografts and xenografts as well as for primate skin and renal allografts (page 224, column 1, paragraph 1).

Hafler et al. teach that anti-CD2 antibodies inhibit T cell responses in human patients with progressive multiple sclerosis (see entire document). In addition to in vivo effects, the in vivo anti-T cell antibodies infusions could be immunosuppressive as determined by in vitro assays (page 136-137, overlapping paragraph). Patients received 0.2 mg /kg antibody in pharmaceutical compositions (see Materials and Methods mAb Infusions). Hafler et al. also teach that T cell-specific antibodies have been used successfully as immunosuppressive reagents in transplant rejections and autoimmune diseases (see Introduction).

Chavin et al. teaches the efficacy of treating allografts and xenografts in vivo with CD2-specific antibodies (see entire document, particularly the Introduction and Discussion). Prolonged allograft survival correlated with suppression of both CTL and NK activity (page 290, column 1, paragraph 3 and Table 2). Chavin et al. teach that anit-human CD2 antibodies have been used in primate models of allografting and have ben found to be effective immunosuppressive agent and that antihuman CD2 antibody may be quite potent in humans (see page 289, column 2, paragraph 1). Previous and current data demonstrate that anti-CD2 antibodies affects a variety of CD4/CD8 T cell dependent response inducing CTL, contact sensitivity, proliferation, IgG responses, tumor immunity, natural killer cytotoxicity and allograft rejection (see page 290, column 1, paragraph 2). Here, Chavin et al. concludes by stating that the ability of anti-CD2 antibodies to suppress lymphocyte precursors and T and non-T cell responses supports its use for induction therapy in transplantation (page 290, last paragraph).

Faustman teaches methods of inhibiting the rejection of allografts and xenografts with T cell-specific antibodies and antibody fragments including the CD2-specificity (see entire document, including column 5, paragraph 1). Such methods of inhibiting rejection include modifying, eliminating and masking an antigen on the surface of a cell (see entire document, including Abstract). In addition, Faustman teaches perfusion with antibodies is carried out by conventional techniques (see column 10, paragraph 1).

Given the in vitro and in vivo observations of potent blocking of various T cell mediated immune responses, including the induction of antigen specific unresponsiveness,

Given the binding and inhibitory properties of the LO-CD2a-specific antibody, including strongly depressing antigen-induced lymphocyte activation and proliferation taught by Xia et al.; one of ordinary skill in the art would have motivated to employ the LO-CD2a in various biological, diagnostic and therapeutic modalities, as taught by the prior art above. It is noted that Xia et al. acknowledged that the ordinary artisan was motivated to employ monoclonal antibodies as attractive reagents for clinical therapeutic use at the time the invention was made (see Introduction on page 310).

Given the teachings of Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman of the art-known potent inhibition of immune responses both in vitro and in vivo by blocking or modulating CD2, one of ordinary skill in the art would have had a reasonable expectation of success that the binding and functional properties of the LO-CD2a antibody specificity would have been consistent with such potent antigen-specific immune responses of the prior art anti-CD2 inhibitory antibodies. Given the prior art teachings of antibody compositions for both in vitro and in vivo regimens employing, characterizing and testing antibodies, including anti-CD2 antibodies, the ordinary artisan would have been motivated to place antibodies with the LO-CD2a specificity in composition form, including in amounts effective to inhibit T cell mediated immune responses, as practiced by the prior art (e.g. see Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman). Also, note that the claimed compositions do not recite a specific amount of anti-LO-CD2a antibodies. It is noted that page 18, paragraph 1 of the instant specification discloses that the scope of the invention is not limited by amounts such as 1 mg. The prior art antibodies including the LO-CD2a antibody specificity do inhibit T cell activation, which is consistent with amounts effective to inhibit T cell mediated immune responses.

It would have prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to generate CD2-specific antibodies including the LO-CD2-specific antibodies to characterize the CD2 specificity and to target said specificity for various biological, diagnostic and therapeutic modalities, as taught by the prior art. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to make and use anti-CD2 antibodies with binding and inhibitory properties,

incorporating well known procedures to make and use anti-CD2 antibodies with the LO-CD2a-specificity, including recombinant antibodies with the ability to elicit alloantigen specific hyporesponsiveness would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing anti-CD2 antibodies with the LO-CD2a antibody specificity.

Again, see the Examiner's Answer, mailed 8/24/00, as well as Section 4 above for a more complete analysis of applicant's arguments and the examiner's rebuttal.

Again, this rejection is consistent with the Decision on Appeal in Ex parte HERVE BAZIN and DOMINIQUE LATINNE, mailed 07/31/2003, of the instant application USSN 09/056,072.

The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965).

Applicant's arguments have not been found persuasive.

6. Double Patenting over U.S. Patent No. 5,951,983.

The following comments have been filed by applicant in the Amendment, filed 11/02/2007.

With respect to the obviousness-type double patenting rejection over Claims 1-4 of U.S. Patent No. 5,951,983, the Examiner is advised that the claimed subject matter of the above-identified application was invented by Herve Bazin and Dominique Latinne prior to the invention of Claims 1-4 of U.S. Patent No. 5,951,983. It is therefore respectfully requested that the obviousness-type double patenting rejection be reconsidered and withdrawn.

However, the terminal disclaimer filed on 02/20/2004, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,951,983 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Further, the obvious-type double patenting rejection was and still is consider proper.

Further, obviousness double patenting has no time limitation, therefore filing a terminal disclaimer is required.

With respect to common ownership at the time the invention was made, the following of record is reiterated.

Claims 30-36 and 38-42 are directed to an invention not patentably distinct from claims 1-4 of commonly assigned U.S. Patent No. 5,951,983. Specifically, the patented claims, which are drawn to a humanized version of the LO-CD2a anti-CD2 antibody anticipates or renders obvious the instant claims for the reasons of record and set forth of record. Although the recitation of the instant and patented claims differ, the patented claims, which are drawn to a humanized version of the LO-CD2a anti-CD2 antibody anticipates or renders obvious the instant claims. Given that the original LO-CD2a antibody was a rat monoclonal antibody, the instantly claimed rat antibody would have been an obvious variant of the patented humanized anti-CD2 antibodies derived from the same starting material. Placing antibodies in composition form for a wide variety of utilities including detection, diagnostic and therapeutic modalities was obvious to the ordinary artisan at the time the invention was made.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 5,951,983, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent Nos. 6,235,525; 6,498,021; 6,552,180 and 6,946,289, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Also, as noted in MPEP 804.03, applicant is reminded that:
Applications or patents are "commonly owned" pursuant to 35 U.S.C. 103(c)(1) if they were wholly or entirely owned by the same person(s), or organization(s)/business entity(ies), at the time the claimed invention was made. See MPEP § 706.02(l)(2) for a detailed definition of common ownership.< Two inventions of different inventive entities come within the >common ownership< provisions of 35 U.S.C. 103(c)>(1)< when:
(A) the later invention is not anticipated by the earlier invention under 35 U.S.C. 102;
(B) the earlier invention qualifies as prior art for purposes of obviousness under 35 U.S.C. 103 against the later invention only under *>subsections< (f) or (g) of 35 U.S.C. 102, or >under< 35 U.S.C. 102(e) for applications >pending on or after December 10, 2004, for reexamination proceedings in which the patent under reexamination was granted on or after December 10, 2004, and for reexamination proceedings in which the patent under reexamination was< filed on or after November 29, 1999; and
(C) the inventions were, at the time the later invention was made, owned by the same person or subject to an obligation of assignment to the same person

Again, applicant is reminded that common ownership means wholly or entirely owned by the same at the time the invention was made and that the patented claims anticipate the instant claims.

It does <u>not</u> appear that applicant has provided a statement regarding the common ownership at the time the invention was made.
Again, applicant should clarify the common ownership at the time the invention was made or provide direction where this statement is in the current record.

7. <u>Double Patenting over U.S. Patent No. 5,730,979</u>.

For the record in contrast to applicant's reliance upon filing a terminal disclaimer over U.S. Patent No. 5,730,9<u>3</u>9;
which is drawn to an Automated Analyzer Having Fluid Abnormalities Detection Device;
the terminal disclaimer filed on 02/20/2004, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,730,9<u>7</u>9 has been reviewed and is accepted.
The terminal disclaimer has been recorded.

8. Claim 44 is deemed allowable.

The LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423 is deemed structurally distinct from the humanized LO-CD2a antibody claimed in U.S. Patent No. 5,951,983.

Also, see USSN 08/477,989, now U.S. Patent No. 5,951,983, where no terminal disclaimer was filed over USSN 08/477,877, now U.S. Patent No. 5,730,979.

9. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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